#### **CLAIMS**

1. A compound of formula (I):

$$R^1$$
  $O$   $N$   $N$   $R^3$   $R^3$ 

5

**(I)** 

wherein:

R<sup>1</sup> and R<sup>2</sup> are independently selected from aryl; and

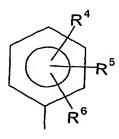
R<sup>3</sup> is hydrogen or alkyl;

or a pharmaceutically acceptable salt or prodrug thereof,

- wherein at least one of R<sup>1</sup> and R<sup>2</sup> has a non-hydrogen substituent in the ortho-position(s) thereof relative to the point of attachment to the [-CH-O-] group.
  - 2. A compound according to claim 1 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected from mono-cyclic aromatic groups.

15

- 3. A compound according to claim 1 or 2 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected from phenyl.
- 4. A compound according to claim 1, 2 or 3 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected
   20 from a group of formula:



wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are independently selected from hydrogen, halo, alkyl, thioalkyl, alkoxy, alkylsulfonyl, amino, mono- and di-alkyl amino, mono- and di-aryl amino, alkylarylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, NR<sup>14</sup>C(O)R<sup>15</sup>, NR<sup>14</sup>SO<sub>2</sub>R<sup>16</sup>,

15

- COOR<sup>15</sup>, OC(O)R<sup>16</sup>, CONR<sup>7</sup>R<sup>8</sup> and SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, wherein R<sup>7</sup> and R<sup>8</sup> are independently selected from hydrogen and alkyl or may form a 5 or 6 membered ring optionally containing 1 or 2 additional heteroatoms selected from N, O and S; and wherein R<sup>14</sup> is selected from H and lower alkyl, R<sup>15</sup> is selected from H, alkyl, aryl and heteroaryl and R<sup>16</sup> is selected from alkyl, aryl and heteroaryl.
- 5. A compound according to claim 1, 2, 3 or 4 wherein R<sup>1</sup> and R<sup>2</sup> are different.
- 6. A compound according to claim 4 or 5 wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are independently selected from fluoro, chloro, bromo and iodo.
  - 7. A compound according to claim 4 or 5 wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are independently selected from alkyl, thioalkyl, alkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl and alkylsulfonyl wherein the alkyl group is selected from lower alkyl.
  - 8. A compound according to claim 4 or 5 wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are independently selected from trifluoromethyl and difluoromethoxy.
- 9. A compound according to claim 4 or 5 wherein one or two of R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are 20 hydrogen.
  - 10. A compound according to claim 4 or 5 wherein R<sup>14</sup> is selected from H.
- 11. A compound according to claim 4 or 5 wherein R<sup>15</sup> and R<sup>16</sup> are independently selected from alkyl.
  - 12. A compound according to claim 4 or 5 wherein R<sup>15</sup> and R<sup>16</sup> are independently selected from lower alkyl.
- 30 13. A compound according to any preceding claim wherein R<sup>3</sup> is selected from alkyl.
  - 14. A compound according to any preceding claim wherein R<sup>3</sup> is selected from tertiary butyl, isobutyl, sec-butyl and isopropyl.

15. A compound according to any preceding claim wherein R<sup>3</sup> is selected from:

### $-(CHR^9)_n(CH_2)_mCR^{10}R^{11}R^{12}$

- 5 wherein n is 0 or 1;
  - m is 0, 1, 2 or 3;
  - R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are selected from hydrogen, alkyl, hydroxy, alkoxy, thioalkyl, amino, mono- and di-alkyl amino, alkoxycarbonyl and R<sup>13</sup>;
- wherein R<sup>13</sup> is selected from aryl, heteroaryl and non-aromatic heterocyclic optionally substituted by one or more groups selected from alkyl, halogen, alkoxy, oxo, aryl, heteroaryl and non-aromatic heterocycle.
  - 16. A compound according to claim 15 wherein m is 0 or 1.
- 15 17. A compound according to claim 15 wherein n is 0.
  - 18. A compound according to claim 13 wherein R<sup>3</sup> is selected from cyclopentyl, cyclohexyl, norbornanyl and adamantyl.
- 20 19. A compound according to claim 1 wherein the compound is selected from:
  - 3-(2,4,4'-trichlorobenzhydryloxy)-N-(tert-butyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(tert-butyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(2-thiophen-2-yl ethyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(cyclopropylmethyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(2,3-dihydrobenzofuran-5-yl-methyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(2,5-dimethylfuran-3-yl-methyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(2,3-Dihydro-benzo[1,4]dioxin-2-yl-methyl) azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(5-methyl-isoxazol-3-yl-methyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-[(R)-sec-butyl]azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-(2-bromothiophen-3-yl-methyl)azetidine-1-carboxamide
  - 3-(2,4'-dichlorobenzhydryloxy)-N-[(S)-sec-butyl]azetidine-1-carboxamide

- 3-(2,4'-dichlorobenzhydryloxy)-N-(thiophen-3-yl-methyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(2-methoxyphenylmethyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(2-furanylmethyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(3-ethoxypropyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(2-tetrahydrofuranylmethyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(exo-2-norbornanyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(1-phenylpropyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-[(R)-a-methylbenzyl]azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-[(R)-1-(3-methoxyphenyl)ethyl]azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-[(S)-1-(3-methoxyphenyl)ethyl]azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(n-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(sec-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(ethyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-[(S)-a-methyl-benzyl] azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(2,2,4-trimethylpent-4-yl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(cyclopentyl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(2,2,4-trimethylpent-4-yl)azetidine-1-carboxamide
- 3-(2,4'-dichlorobenzhydryloxy)-N-(2-methylbut-2-yl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-2'-fluoro-4'-bromobenzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(methylthio)benzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(methylthio)benzhydryloxy]-N-(iso-propyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(methylthio)benzhydryloxy]-N-(sec-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(methylthio)benzhydryloxy]-N-(benzyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4-fluoro-4'-chlorobenzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4-fluoro-4'-chlorobenzhydryloxy]-N-(iso-propyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4-fluoro-4'-chlorobenzhydryloxy]-N-(sec-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4-fluoro-4'-chlorobenzhydryloxy]-N-(cyclohexyl)azetidine-1-

WO 2004/096763 PCT/GB2004/001831

#### carboxamide

- 3-[2-(trifluoromethyl)-4-fluoro-4'-chlorobenzhydryloxy]-N-(benzyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)benzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)benzhydryloxy]-N-(iso-propyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)benzhydryloxy]-N-(sec-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)benzhydryloxy]-N-(cyclohexyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)benzhydryloxy]-N-(benzyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(trifluoromethoxy)benzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(trifluoromethoxy) benzhydryloxy]-N-(iso-propyl) azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(trifluoromethoxy)benzhydryloxy]-N-(sec-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(trifluoromethoxy)benzhydryloxy]-N-(benzyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(1-adamantyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(cyclohexyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(tert-amyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-methylbenzhydryloxy]-N-(1-adamantyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-methylbenzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-methylbenzhydryloxy]-N-(cyclohexyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-methoxybenzhydryloxy]-N-(1-adamantyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-methoxybenzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-fluorobenzhydryloxy]-N-(1-adamantyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-fluorobenzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-fluorobenzhydryloxy]-N-(cyclohexyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(allyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(methylthio)benzhydryloxy]-N-(1-adamantyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(methylthio)benzhydryloxy]-N-(cyclohexyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(difluoromethoxy)benzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(difluoromethoxy)benzhydryloxy]-N-(sec-butyl)azetidine-1-

carboxamide

10

- 3-[2-(trifluoromethyl)-4'-(difluoromethoxy) benzhydryloxy]-N-(iso-propyl) azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(difluoromethoxy)benzhydryloxy]-N-(cyclohexyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-(difluoromethoxy)benzhydryloxy]-N-(allyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-fluorobenzhydryloxy]-N-(sec-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-4'-fluorobenzhydryloxy]-N-[(S)-a-methylbenzyl]azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-2'-fluoro-4'-(1-piperidinyloxomethyl)benzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide
- 3-[2-(trifluoromethyl)-2'-fluorobenzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide, and 3-[(S\*)-2-(trifluoromethyl)-4'-chlorobenzhydryloxy]-N-(tert-butyl)azetidine-1-carboxamide.
- 20. For use in therapy, a compound according to any one of claims 1 to 19.
- 21. Use of a compound according to any of claims 1 to 19 in the manufacture of a medicament for the treatment of a disorder mediated by CB<sub>1</sub> receptors.
- 22. A method of treatment of a disorder mediated by CB<sub>1</sub> receptors comprising administration to a subject in need of such treatment an effective dose of a compound of formula (I) as defined in any of claims 1 to 19, or a pharmaceutically acceptable salt or prodrug thereof.
- 23. A use or method according to claim 22 wherein the compound of formula (I) is in oral medicament.
- 15 24. A use or method according to claim 21 or 22 wherein the disorder is selected from psychosis, memory deficit, cognitive disorders, attention deficit disorder, migraine, neuropathy, neuro-inflammatory disorders, cerebral vascular injuries, head trauma, anxiety disorders, depression, stress, epilepsy, dementia, distonia, Alzheimer's disease, Huntingdon's disease, Tourette's syndrome, ischaemia, pain, Parkinson's disease, 20 schizophrenia, substance abuse disorders, smoking cessation, treatment of nicotine

dependance and/or treatment of symptoms of nicotine withdrawal, gastrointestinal disorders, eating disorders associated with excessive food intake, and non-insulin dependant diabetes mellitus.

- 5 25. A use or method according to claim 24 wherein said substance abuse disorder is abuse of nicotine, alcohol and/or opiates.
  - 26. A use or method according to claim 24 wherein said eating disorder is obesity.
- 10 27. A use or method according to claim 24 wherein said disorder is Parkinson's Disease.
  - 28. A use or method according to claim 24 for smoking cessation.
- 15 29. A use or method according to claim 24 for gastrointestinal disorders.
- 30. A use or method according to claim 24 wherein said disorder is selected from psychosis, schizophrenia, cognitive disorders, attention deficit disorder, smoking cessation, gastrointestinal disorders, eating disorders associated with excessive food intake, and non-insulin dependant diabetes mellitus.

# This Page is inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

	BLACK BORDERS
	IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
	FADED TEXT OR DRAWING
	BLURED OR ILLEGIBLE TEXT OR DRAWING
	SKEWED/SLANTED IMAGES
	COLORED OR BLACK AND WHITE PHOTOGRAPHS
	GRAY SCALE DOCUMENTS
	LINES OR MARKS ON ORIGINAL DOCUMENT
۵	REPERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
	OTHER:

IMAGES ARE BEST AVAILABLE COPY.
As rescanning documents will not correct images problems checked, please do not report the problems to the IFW Image Problem Mailbox